

Application No.: 10/733,782
Response dated: August 8, 2006
Reply to Office Action dated: March 8, 2006

Amendments to the Drawings:

The attached sheets of drawings includes changes to Figures 11-15. The sheets, which include Figures 11-15 replace the original sheets including Figure 11-15. Figures 11-15 previously omitted sequence identification numbers.

Attachment: Replacement sheets
Annotated Sheets Showing Changes

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Remarks/Arguments

By a non-final Office Action dated March 8, 2006 the Examiner in charge of this case rejected the claims of this application on a variety of grounds. Claims 1-36 are currently pending in the application; Claims 3, 14, and 29-32 have been withdrawn from consideration as being drawn to a non-elected invention; Claims 1, 4-12, and 33-35 are rejected under 35 U.S.C. 112, 1st and 2nd paragraph and Claims 1, 2, 4, 5, 33 and 34 are rejected under 35 U.S.C. 102(b). The applicants have responded by submitting the amendments and comments set forth hereinbelow. Based on this submission, reconsideration of the merits of this patent application is respectfully requested.

Claim Amendments

Claims 9-13, 16, 22, 23 and 27 are amended to more clearly layout the type of deletion mutants claimed by the present invention, as well as to correct minor clerical errors. Claims 1-8, 28 and 33-34 are canceled without prejudice or disclaimer, thus rendering the Examiner's objections to these claims moot. Also, applicants have included new Claims 37-44 drawn to specific embodiments of the double mutant RecA protein and related kits. Support for these claim amendments are found for example, throughout the specification, specifically at Example 3, [00074]; page 5, [0033], and Example 6, [00081]. No new matter is added by the introduction of these claims.

Election/Restrictions

Although applicants continue to traverse the Examiner requirement for restriction, the finality of the requirement is acknowledged. Accordingly, applicants wish to reserve the right to file a divisional application drawn to the non-elected claims and/or to rejoin process Claims 29-32 once the product claims are found allowable.

Sequence Rules

Figures 11-15 are objected to for containing sequences not identified by a SEQ ID No. in the figures or in the Brief Description of the Drawings. The specification is amended to include the requisite sequence identifiers. A separate substitute specification and a marked-up copy of the substitute specification containing these amendments are submitted herewith. Applicants

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submit that with the introduction of the specific sequence identifiers in the substitute specification, no new matter is added.

Double Patenting

Claims 22 and 23 along with Claims 27 and 28 are objected to under 37 CFR 1.75 as covering substantially the same claim scope. Without acquiescing to the objection, to obviate this issue, Claims 22 is amended herein to refer to the most preferable pH for reducing complete product formation. Also, Claim 28 is canceled herein. The text of Claim 28 is incorporated into Claim 27.

Claim Objections

Claims 1 and 9 are objected to for inappropriately using the plural form of the term "acids." Although Claim 1 is canceled, the term "acid" in Claim 9 is corrected herein to reflect the singular form.

Claim Rejections 35 USC §112

Claims 1, 4-12, and 33-35 are rejected under 35 USC 112, second paragraph, as being indefinite for various reasons. At the outset, applicants submit that Claims 1-8 and 33-34 are canceled without prejudice, thus rendering the rejections to these claims moot. Claims 9 and 10 are amended to make clear that the double mutant RecA protein is truncated by at least 13-25 amino acid residues at the C-terminal end of the protein.

Claims 6-8 and 22-23 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserts that applicants only disclose the $\Delta C17/E38K$ RecA mutant as having the enhancement of strand exchange function, and that this mutant induces "complete" strand exchange at pH 8.3 and 8.8, but not at 8.0 or 9.3 (see Figs. 8 and 9). Furthermore, the Examiner asserts that the instant disclosure does not describe enough functional species in order to be commensurate with the claimed genus. Applicants traverse this rejection.

In response, applicants submit that Claims 1-8 are canceled herein without prejudice, rendering the rejections to Claims 6-8 moot. As to Claims 22-23, applicants submit that these claims are amended to more clearly reflect the most suitable pH range (pH of 8.0 to 9.0) and a preferred pH of 8.5, respectively for inducing "complete" strand exchange.

Furthermore, applicants submit that rejection based on a lack of written description is unwarranted. Applicants can see no reason why a person of ordinary skill in the art upon reading the specification as a whole could not readily make the claimed double mutant RecA proteins and use the mutant proteins to produce a desired utility commensurate in scope with the claimed invention.

For example, the specification describes the generation, expression and purification of a representative set of C-terminal truncations of the RecA protein, where 6, 13, 17 and 25 amino acid residues are progressively removed. These truncations remove 3, 6, and 7 of the negatively charged amino acid residues in the far C-terminal domain of the RecA protein (defined in the specification as residues 328 to 352). The 25 amino acid residues at the C-terminal of RecA exhibit a preponderance of negatively charged amino acids, with seven Glu or Asp residues in the terminal 17 residues. The specification also describes a point mutation, the replacement of an acidic residue with a basic residue at position 38 in the RecA protein. (See for example, pg. 4 [00018]; pg. 7, [00049] and [00052]; and Example 6).

The combination of these RecA C-terminal truncations 13-25 (more preferably 13-17 amino acid residues) and the point mutation at position 38 is described in the specification to facilitate one skilled in the art with constructing the claimed RecA double mutant. Based on the experiments described in the specification, applicants believe that the RecA truncation and basic point mutation at position 38 work together in a double mutant to eliminate a discernible lag in single stranded DNA binding protein (SSB) displacement. This process of enhancing RecA's capacity to displace SSB and increasing the steady-state level of DNA binding by RecA is believed to be pH and Mg^{+2} concentration dependent. (See for instance Examples 8 and 12-14; Figures 3, and 8-10 and [000112]).

Furthermore, in the specification, applicants propose that the negative charges of the C-terminus are part of a regulatory network of protein surface salt bridges. It is believed that the increase in SSB displacement and overall DNA binding observed when the deletion of the C-terminal 17 residues and the replacement of an acidic residue with a basic residue at position 38 are combined could also reflect particular disruptions of an extensive salt bridge network. Hence, the double mutant appears to bind to DNA better in the presence of SSB than in its absence. (See for example, pgs. 25-26, [000110-112]). Applicants believe that that upon reading the specification as a whole one could readily (1) construct the claimed double mutant RecA proteins, (2) correlate the structure of the RecA double mutant with its function as described in

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the specification, and (3) use the double mutants to produce a desired utility commensurate in scope with the claimed invention (i.e., enhance binding to DNA during a strand exchange reaction, and completion of the reaction, relative to wild-type RecA). Accordingly, applicants believe that the specification sufficiently describes the claimed invention.

Claim Rejections 35 USC §102

Claims 1, 2, 4, 5, 33 and 34 are rejected under 35 USC §102(b) as being anticipated by Tateishi et al. (J. Mol. Biol., 1992) and Larminat et al. (Mol. Gen. Genet., 1989). Specifically, the Examiner asserts that Tateishi et al. discloses a *E. Coli* RecA (RecA5327) with a 25 amino acid C-terminal truncation and Larminat et al. discloses a *E. Coli* RecA (RecA335) with a 17 amino acid C-terminal truncation. In response, applicants submit that Claims 1-8 and 33-34 are canceled herein without prejudice, rendering the rejections moot.

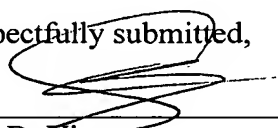
Claim Objections

Claims 13, 15-21, 24-27 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. Applicants have rewritten Claims 13 and 36 as new independent Claims 39 and 40.

Accordingly, applicants respectfully request that in view of these claim amendments and comments, the rejection be respectfully reconsidered, withdrawn and that a timely Notice of Allowance be issued in this case.

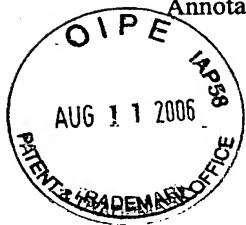
A petition for an extension of time is included herewith. Please charge the extension fee to Deposit Account No. 17-0055. If any other fee is due in this or any subsequent response, please consider this to be a request to charge the fee required to effectuate this response to Deposit Account No. 17-0055.

Respectfully submitted,



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Title: RecA MUTANTS

Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger

Application No.:

Docket Number: 960296.99501

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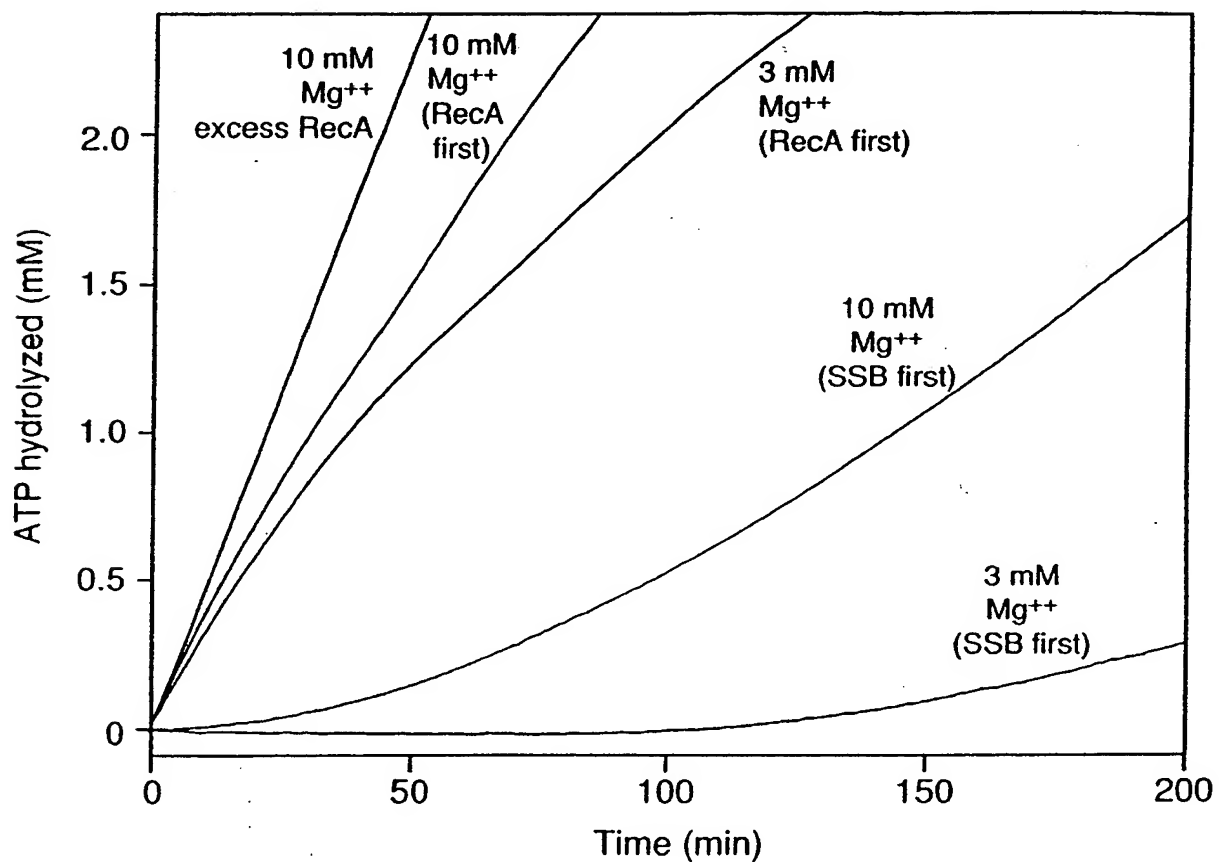


FIG 1

Title: RecA MUTANTS

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Application No.:

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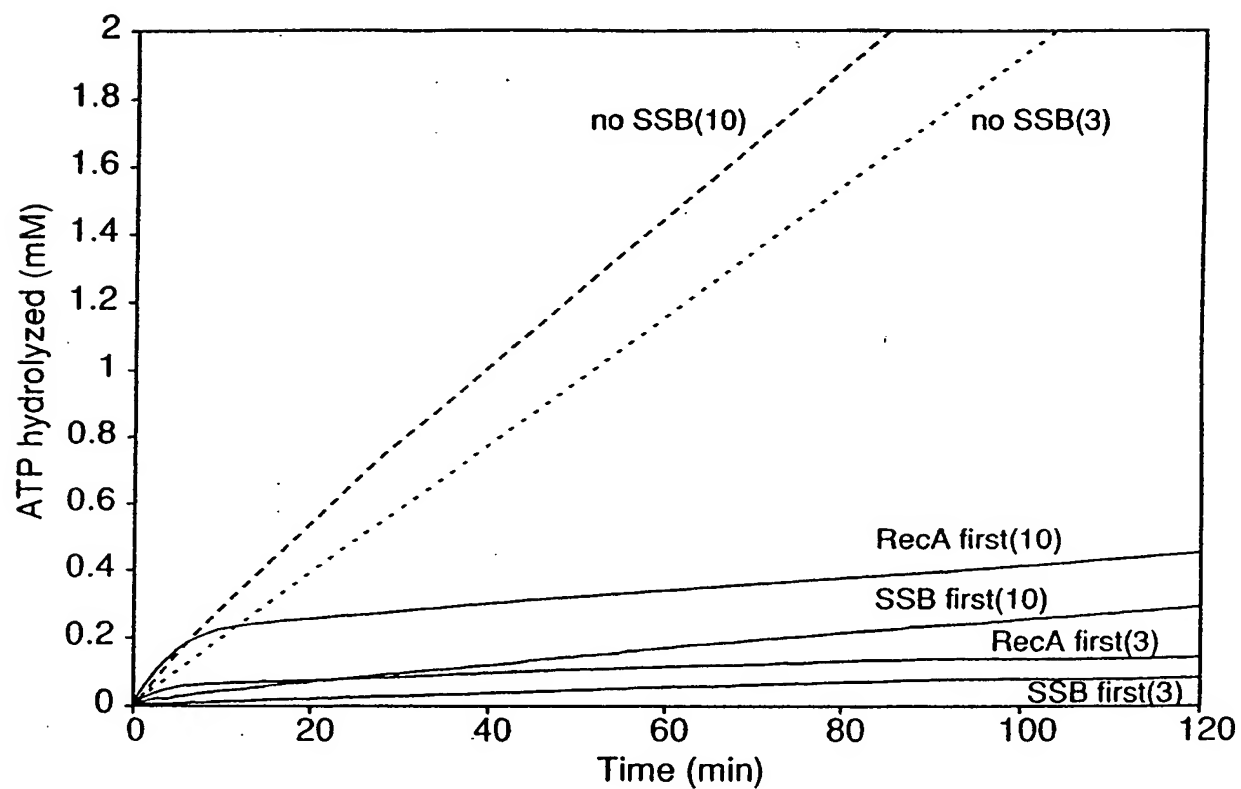


FIG 2

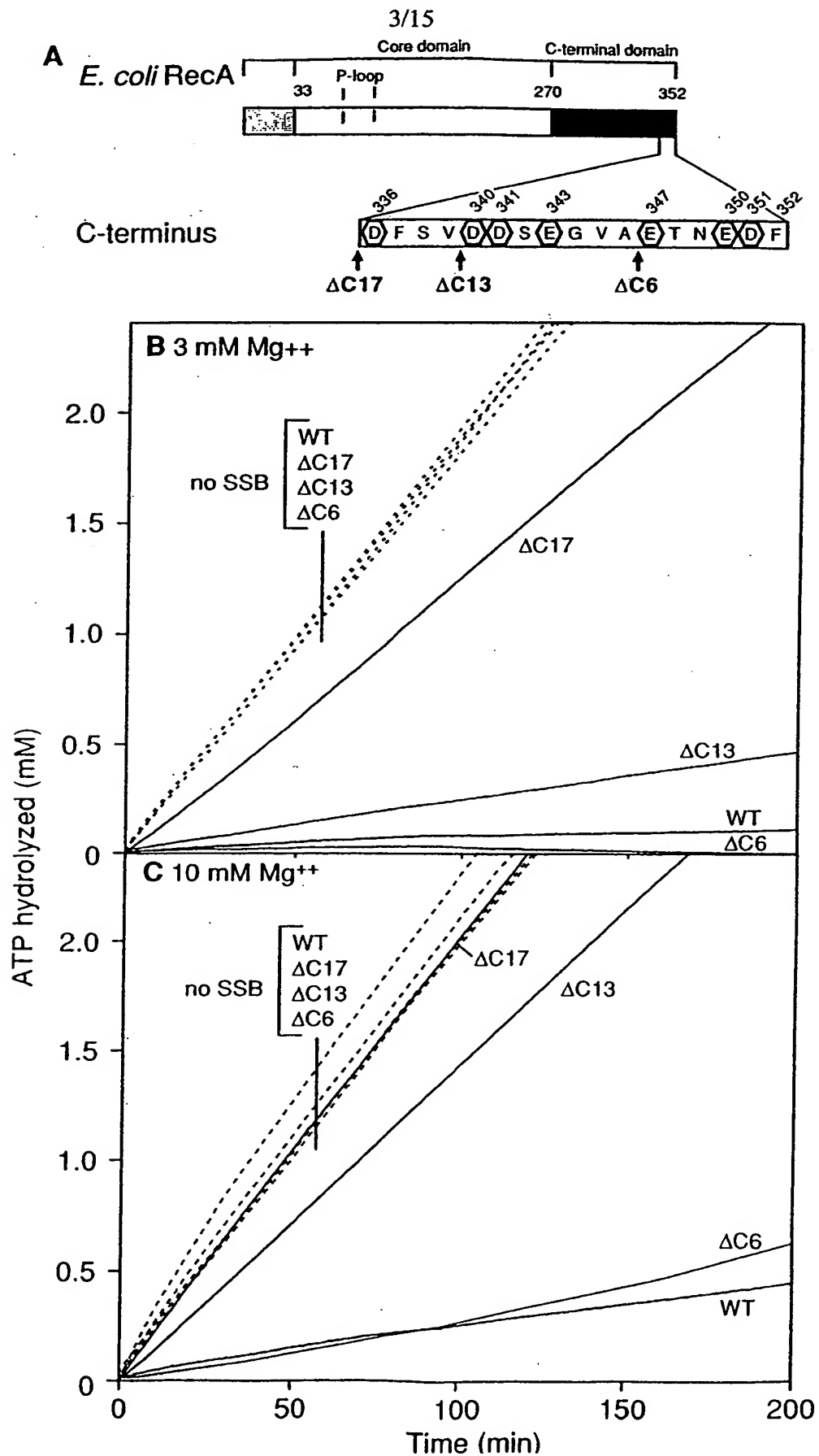


FIG 3

Title: RecA MUTANTS

Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Eggler

Application No.:

Docket Number: 960296.99501

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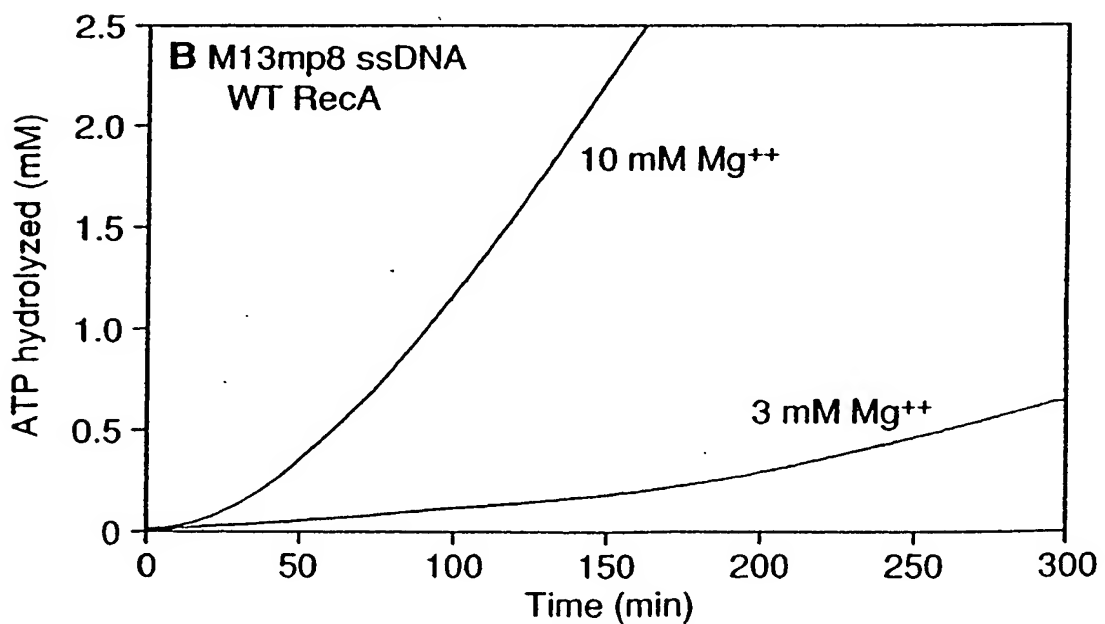
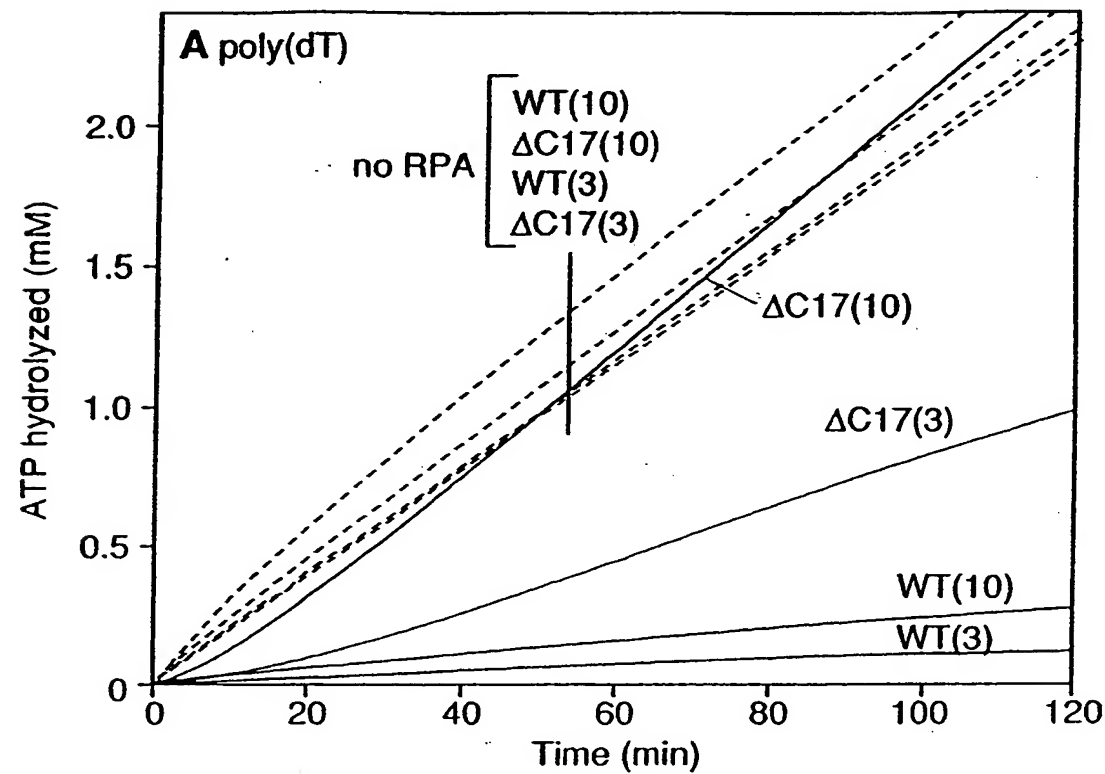


FIG 4

Title: RecA MUTANTS

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Application No.:

Docket Number: 960296.99501

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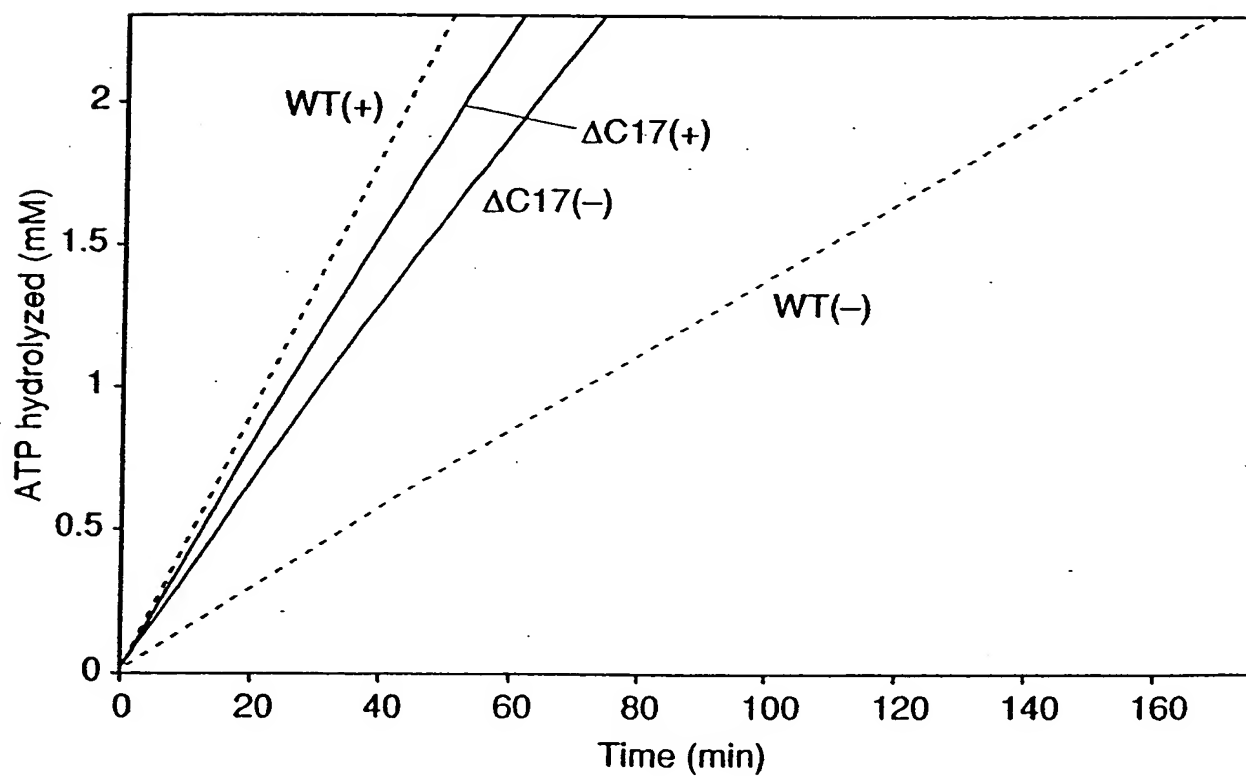


FIG 5

Title: RecA MUTANTS

Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger

Application No.:

Docket Number: 960296.99501

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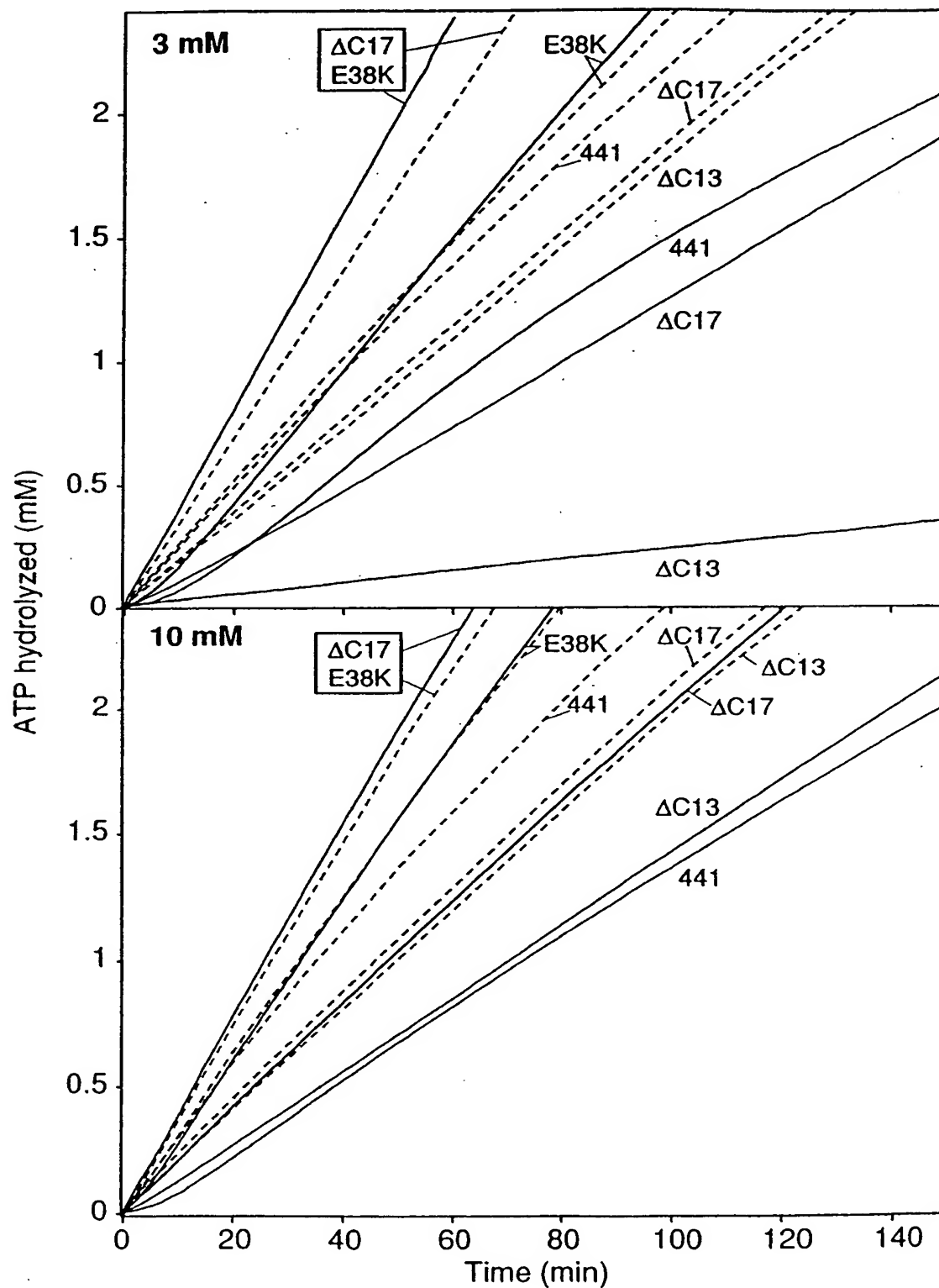


FIG 6

Title: RecA MUTANTS

Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egler

Application No.:

Docket Number: 960296.99501

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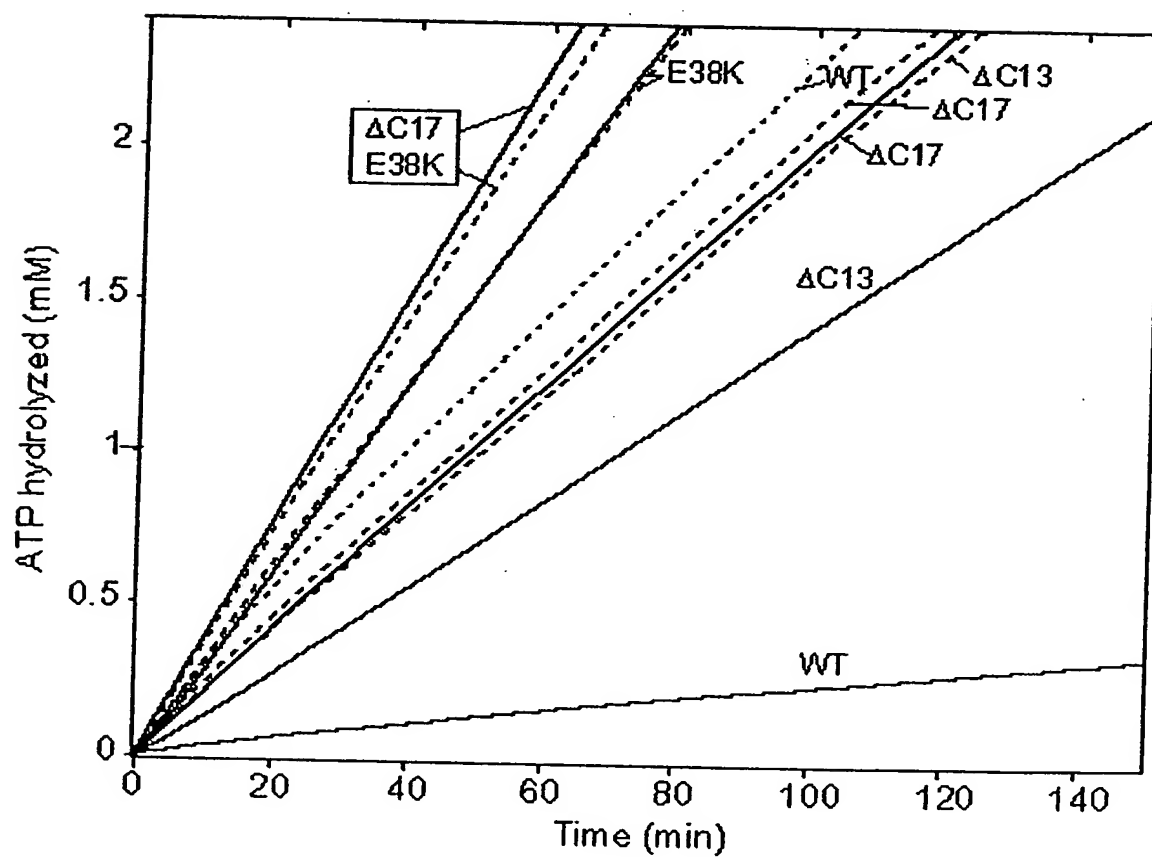


FIG 7

Title: RecA MUTANTS
Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger
Application No.:
Docket Number: 960296.99501

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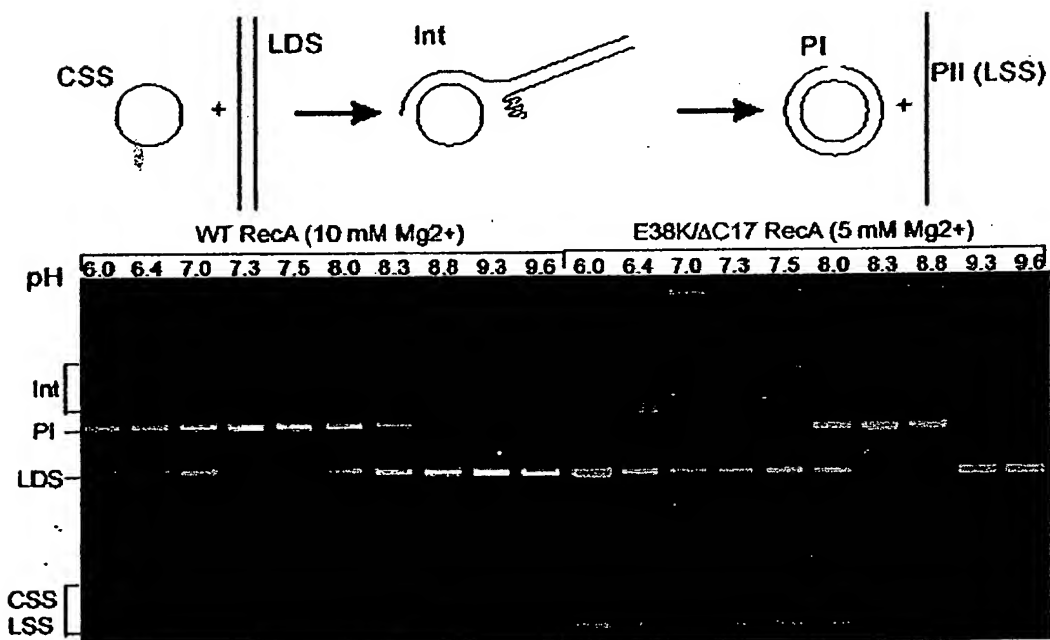


FIG 8

Title: RecA MUTANTS
Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger
Application No.:
Docket Number: 960296.99501

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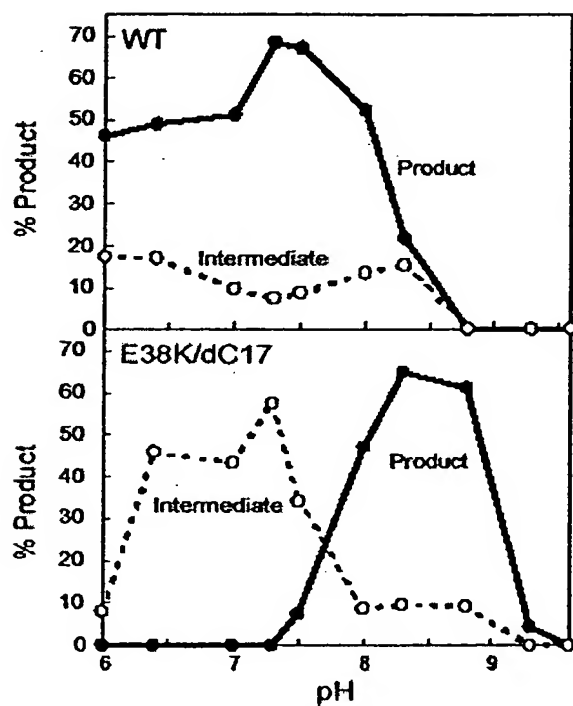


FIG 9

Title: RecA MUTANTS
Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Eggler
Application No.:
Docket Number: 960296.99501

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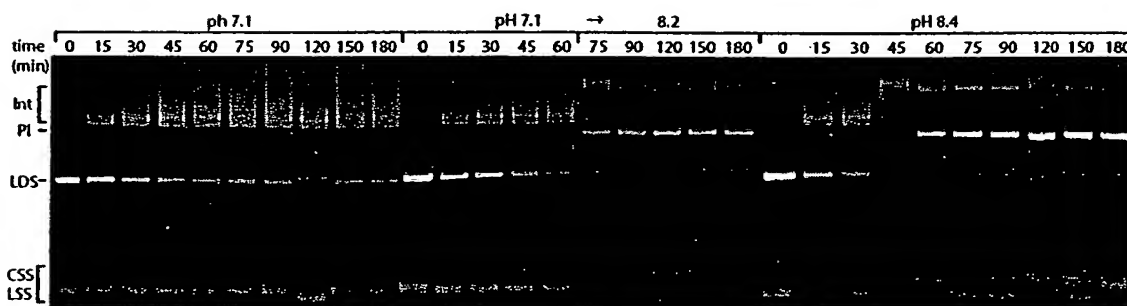


FIG 10

Title: RecA MUTANTS

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Application No.:

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AIDENKQKA LAAALGQIEK QFGKGSIMRL GEDRSMDVET ISTGSLSLDI
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TPKAEIEGEI GDSHMGLAAR MMSQAMRKLA GNLKQSNTLL IFINQIRMKI
GVMFGNPETT TGGNALKFYA SVRLDIRRIG AVKEGENVVG SETRVKVVKN
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QGKANATAWL KDNPETAKEI EKKVRELLLS NPNSTP SEQ ID NO:1

FIG 11

Title: RecA MUTANTS

Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger

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51  GATTGAGAAA CAATTTGGTA AAGGCTCCAT CATGCGCCTG GGTGAAGACC
101 GTTCAATGGA TGTGGAAACC ATCTCTACCG GTTCGCTTTC ACTGGATATC
151 GCGCTTGGGG CAGGTGGTCT GCCGATGGGC CGTATCGTCG AGATCTACCG
201 ACCGGAATCT TCCGGTAAAA CCACGCTGAC GCTGCAGGTG ATCGCCGCAG
251 CGCAGCGTGA AGGTAAAACC TGTGCGTTTA TCGATGCTGA ACACGCGCTG
301 GACCCAATCT ACGCACGTAA ACTGGGCGTC GATATCGACA ACCTGCTGTG
351 CTCCCAGCCG GACACCGGCG AGCAGGCACT GGAAATCTGT GACGCCCTGG
401 CGCGTTCTGG CGCAGTAGAC GTTATCGTCG TTGACTCCGT GCGGGCACTG
451 ACGCCGAAAG CGGAAATCGA AGGCGAAATC GGCGACTCTC ACATGGGCCT
501 TCGGGCACGT ATGATGAGCC AGGCGATGCG TAAGCTGGCG GGTAACCTGA
551 AGCAGTCCAA CACGCTGCTG ATCTTCATCA ACCAGATCCG TATGAAAATT
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901 CAGGGTAAAG CGAATGCGAC TGCCTGGCTG AAAGATAACC CGGAAACCGC
951 GAAAGAGATC GAGAAGAAAG TACGTGAGTT GCTGCTGAGC AACCCGAAct
1001 CAACGCCGTA A  SEQ ID NO:2
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FIG 12

Title: RecA MUTANTS
Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger
Application No.:
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AIDENKQKA LAAALGQIEK QFGKGSIMRL GEDRSMDVKT ISTGSLSLDI
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TPKAEIEGEI GDSTMGLAAR MMSQAMRKLA GNLKQSNTLL IFINQIRMKI
GVMFGNPETT TGGNALKFYA SVRLDIRRIG AVKEGENVVG SETRVKVVKN
KIAAPFKQAE FQILYEGIN FYGELVDLGV KEKLIEKAGA WYSYKGEKIG
QGKANATAWL KDNPETAKEI EKKVRELLLS NPNSTP* SEQ ID NO:3

FIG 13

Title: RecA MUTANTS
Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egglar
Application No.:
Docket Number: 960296.99501

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451 ACGCCGAAAG CGGAAATCGA AGGCGAAATC GGCGACTCTC ACATGGGCCT
501 TCGGCGACGT ATGATGAGCC AGGCGATGCG TAAGCTGGCG GGTAACCTGA
551 AGCAGTCCAA CACGCTGCTG ATCTTCATCA ACCAGATCCG TATGAAAATT
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701 AGGGCGAAAA CGTGGTGGGT AGCGAAACCC GCGTGAAAGT GGTGAAGAAC
751 AAAATCGCTG CGCCGTTTAA ACAGGCTGAA TTCCAGATCC TCTACGGCGA
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851 TGATCGAGAA AGCAGGCGCG TGGTACAGCT ACAAAGGTGA GAAGATCGGT
901 CAGGGTAAAG CGAATGCGAC TGCCTGGCTG AAAGATAACC CGGAAACCGC
951 GAAAGAGATC GAGAAGAAAG TACGTGAGTT GCTGCTGAGC AACCCGAACT
1001 CAACGCCGTA A      SEQ ID NO:4
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FIG 14

Title: RecA MUTANTS
Inventor(s): Michael M. Cox/Shelley L. Lusetti/Aimee L. Egger
Application No.:
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KIAAPFKQAE FQILYEGIN FYGELVDLGV KEKLIEKAGA WYSYKGEKIG
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SEQ ID NO: 5